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| EXAMINER | |
|---|---|
| ROONEY, NORA MAUREEN | |
| ART UNIT | PAPER NUMBER |
| 1644 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

SIP_Docket@mwe.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/038,509 | SMITH ET AL. | |
| | Examiner | Art Unit | |
| | NORA M. ROONEY | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,6,7 and 9-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 6-7 and 9-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application.
6) ☐ Other: _____.

**DETAILED ACTION**

1. Applicant's response filed on 01/06/2010 is acknowledged.

2. Claims 1, 3, 6-7 and 9-11 are currently pending and under consideration as they read on a method of detecting Graves disease in a patient comprising obtaining a biological sample from the patient and measuring the binding of disease specific IgG with IGF-1 receptor relative to a control wherein an elevated level of IgG IgF-1 binding relative to the control indicates Graves disease.

***Double Patenting***

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 3, 6-7 and 9-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,936,426 (PTO-892; Reference A). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of detecting Graves' disease in a patient comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient, and (b) detecting in said orbital or skin sample the activation of fibroblasts by binding of disease specific IgG to the IGF-1 receptor (IGF-1R) relative to a control wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease and wherein fibroblast activation is determined by measuring the level of IL-16 expressed by said IgG-activated fibroblasts, RANTES expressed by said IgG-activated fibroblasts or by measuring T cell migration towards said fibroblasts in said orbital or skin sample of claim 1; a method of detecting the presence of antibody-activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for IL-16 (c) detecting the level of IL-16 released by said fibroblasts relative to

a control, wherein an elevated level of IL-16 detects the presence of antibody-activated fibroblasts of claim 9; a method of detecting the presence of antibody-activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for RANTES; (c) detecting the level of RANTES released by said fibroblasts relative to a control, wherein an elevated level of RANTES detects the presence of antibody-activated fibroblasts of claim 10; and a method of detecting the presence of antibody-activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with antibodies specific for IL-16 and RANTES; (c) detecting the levels of IL-16 and RANTES released by said fibroblasts relative to a control, wherein an elevated level of both IL-16 and RANTES detects the presence of antibody-activated fibroblasts of claim 11; and Claims 1-4 of U. S. Patent 6,936,426 are directed to a method of detecting thyroid-associated ophthalmopathy in a patient comprising: obtaining a biological sample from the patient, isolating IgG from the patient sample, exposing the IgG to orbital fibroblasts from patients with thyroid-associated ophthalmopathy, measuring the level of IL-16 or RANTES produced by the orbital fibroblasts, wherein an elevated level of IL-16 or RANTES, as compared to normal control indicates the presence or severity of thyroid-associated ophthalmopathy in the patient of claim 1; wherein the level of IL-16 or RANTES is measured by an Enzyme-Linked Immunosorbent Assay (ELISA) of claim 2; wherein the patient is human of claim 3; and wherein the biological sample is selected from the group consisting of: blood, synovial fluid, ascites, and tissue of claim 4. It is noted that thyroid-associated opthalmopathy is present in Graves Disease patients. Therefore, the same method is being performed in the same patient population for the same result.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 3, 6-7 and 9-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: a method of detecting Graves' disease in a human patient comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient, and (b) detecting fibroblast activation by IGF-1 receptor (IGF-1R) IgG autoantibodies in said orbital or skin sample by measuring IL-16, RANTES or T cell migration towards said fibroblasts in said orbital or skin sample, wherein an increased presence of fibroblasts activated by IGF-1 receptor (IGF-1R) IgG autoantibodies in said orbital or skin sample compared to control indicates Graves disease; a method of detecting the presence of IGF-1 receptor (IGF-1R) IgG autoantibody-activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for IL-16 (c) and detecting the level of IL-16 released by said fibroblasts relative to a control, wherein an elevated level of IL-16 detects the presence of IGF-1 receptor (IGF-1R) IgG autoantibody-activated fibroblasts; a method of detecting the presence of IGF-1 receptor (IGF-1R) IgG autoantibody-activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for RANTES; and (c) detecting the level of RANTES released by said fibroblasts relative to a control, wherein an elevated level of RANTES detects the presence of IGF-1

receptor (IGF-1R) IgG autoantibody-activated fibroblasts; a method of detecting the presence of IGF-1 receptor (IGF-1R) IgG autoantibody activated fibroblasts, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with antibodies specific for IL-16 and RANTES; and (c) detecting the levels of IL-16 and RANTES released by said fibroblasts relative to a control, wherein an elevated level of both IL-16 and RANTES detects the presence of IGF-1 receptor (IGF-1R) IgG autoantibody-activated fibroblasts. The specification does not provide reasonable enablement for : **a method of detecting Graves' disease in a patient** comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient, and (b) detecting in said orbital or skin sample **the activation of fibroblasts by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)** relative to a control wherein an increased presence of **IgG-activated fibroblasts** compared to the control indicates Graves' disease and wherein fibroblast activation is determined by measuring the level of IL-16 expressed by said IgG-activated fibroblasts, RANTES expressed by said IgG-activated fibroblasts or by measuring T cell migration towards said fibroblasts in said orbital or skin sample of claim 1; a method of **detecting the presence of antibody-activated fibroblasts**, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for IL-16 (c) detecting the level of IL-16 released by said fibroblasts relative to a control, wherein an elevated level of IL-16 **detects the presence of antibody-activated fibroblasts** of claim 9; a method of **detecting the presence of antibody-activated fibroblasts**, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with an antibody specific for RANTES; (c) detecting the level of RANTES released by said fibroblasts relative to

a control, wherein an elevated level of RANTES **detects the presence of antibody-activated fibroblasts** of claim 10; and a method of **detecting the presence of antibody-activated fibroblasts**, said method comprising (a) obtaining an orbital or skin sample comprising fibroblasts from the patient; (b) contacting said sample with antibodies specific for IL-16 and RANTES; (c) detecting the levels of IL-16 and RANTES released by said fibroblasts relative to a control, wherein an elevated level of both IL-16 and RANTES **detects the presence of antibody-activated fibroblasts** of claim 11 and as applied to claims 3 and 6. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

Applicant's arguments filed on 01/06/2010 have been fully considered, but are not found persuasive.

Applicant argues:

> "Essentially, the Office contends that the claimed method of detecting Graves' disease in a human patient is enabled only for measuring the levels of RANTES or IL-16 or by measuring fibroblast activation. While Applicant respectfully maintain that the specification enables the full scope of the claimed invention, base claim 1 has been amended to recite the embodiments indicated in the Office Action to be enabled, rendering moot the rejection."

It is the Examiner's position that the claims, as recited, do not require the active step of contacting disease specific IgG to the IGF-1 receptor in claims 1, 3 and 6-7, nor do claims 9-11 require that the antibody be contacted with fibroblasts. As such, the claimed methods do not detect Graves' disease in a patient or the presence of antibody activated fibroblasts. The present claims are directed to obtaining a sample of skin or orbital fibroblasts from any patient and measuring IL-16, RANTES or T cell migration as a measure of the activation of fibroblasts and

comparing the level to a control. As such, there is no active step of contacting with antibody in vitro or in vivo. Rather, the claims recite that by measuring IL-16, RANTES and T cell migration, one is detecting antibody-activated fibroblasts. Since IL-16, RANTES and T cell migration are not specific to Graves Disease fibroblasts or antibody-activated fibroblasts, the recited method is unpredictable to detect Graves Disease or antibody activation.

The specification discloses a method of detecting Graves disease or rheumatoid arthritis in a human patient comprising contacting an antibody sample with a fibroblast sample from the same patient and measuring the IL-16 and/or RANTES levels that are induced by Graves' disease specific IgG activation of the IGF-1R on the fibroblast, whereby increased expression of either cytokine is associated with the presence of disease specific IgG and is an indicator of disease; and a method of detecting Graves disease or rheumatoid arthritis in a human patient comprising: contacting an antibody sample with a fibroblast sample from the same patient; exposing a NWNA-T cell to the activated fibroblast using a Boyden chamber; measuring the T cell migration toward the activated fibroblast, and determining that positive T cell migration indicates IL-16 and/or RANTES expression in disease-specific IgG-activated fibroblasts through their IGF-1R, whereby increased expression of either cytokine is associated with the presence of disease specific IgG.

The Examiner suggests that Applicant amend the claims to recite the active step of contacting the fibroblasts with antibody. However, even with an antibody contact step added to the claims, the specification is not enabled for a method of detecting Graves disease by measuring fibroblasts that are activated by "disease specific IgG to the IGF-1 receptor (IGF-

1R)." The term "disease specific" is not limited to any particular disease and as such is not enabled for use in detecting Graves Disease. The antibodies must necessarily be Graves' Disease specific to be enabled for use in the claimed invention of specifically detecting Graves Disease. Further, the specification is not enabled for the use of any "IgG to the IGF-1 receptor (IGF-1R)." Rather, the only enabled source of the "IgG to the IGF-1 receptor (IGF-1R)" is the same patient. Therefore, the antibody is an IgG autoantibody to the IGF-1 receptor (IGF-1R). The claims as currently recited may be read to include the additional limitation of activating fibroblasts by binding of Graves Disease specific IgG to the IGF-1 receptor (IGF-1R). However, since the claims are limited to disease detection in patients that are the source of the fibroblasts, the enabled method does not actually require IgG to the IGF-1 receptor (IGF-1R) at all. Rather, the method only requires fibroblasts to have been activated by IgG autoantibody to the IGF-1 receptor (IGF-1R) in vivo or in vitro. A method which reads on any IgG to the IGF-1 receptor (IGF-1R) is not enabled since the disease is detected using the fibroblasts, not the IgG to the IGF-1 receptor (IGF-1R). In the same way, the specification is also not enabled for a method of detecting "antibody activated" fibroblasts. The specification is enabled for the detection of Graves Disease specific IgG to the IGF-1 receptor (IGF-1R) activated fibroblasts.

***Claim Rejections - 35 USC § 102***

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 3, 6-7 and 9-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Sciaky et al. (IDS filed on 11/04/2002).

Sciaky et al. teaches a method comprising obtaining an orbital sample comprising fibroblasts from a human patient, and detecting the activation of fibroblasts by measuring the level of IL-16 expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for IL-16, RANTES expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for RANTES and T cell migration towards said fibroblasts by exposing T-cells to said orbital sample comprising said fibroblasts and measuring T-cell migration toward said fibroblasts in said orbital sample relative to a normal control patients (In particular, page 3807, whole document).

The recitations of "a method of detecting Graves' Disease," "by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)" and "wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease" of claim1; "wherein an elevated level of the marker compared to the control indicates presence of said IgG-activated fibroblasts" of claim 3; "wherein an increase in the migration of said fibroblasts relative to the control indicates presence of said IgG-activated fibroblasts" of claim 6; and"detecting the presence of antibody-activated fibroblasts" and "detects the presence of antibody-activated

fibroblasts" of claims 9-11 are inherent in the reference method. The same methods steps are being performed using the same sample (orbital fibroblasts) from the same patients (human patients), so the same result must necessarily occur.

The reference teachings anticipate the claimed invention.

9. Claims 1, 3, 7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Blaschke et al. (PTO-892; Reference U).

Blaschke et al. teaches a method comprising obtaining an skin sample comprising fibroblasts from a human patient, and detecting the activation of fibroblasts by measuring the level of IL-16 expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for IL-16, (In particular, paragraph spanning pages 658-659, first full paragraph on page 659, Table I, whole document).

The recitations of "a method of detecting Graves' Disease," "by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)" and "wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease" of claim1; "wherein an elevated level of the marker compared to the control indicates presence of said IgG-activated fibroblasts" of claim 3; and "detecting the presence of antibody-activated fibroblasts" and "detects the presence of antibody-activated fibroblasts" of claim 9 are inherent in the reference

method. The same methods steps are being performed using the same sample (skin fibroblasts) from the same patients (human patients), so the same result must necessarily occur.

The reference teachings anticipate the claimed invention.

10. Claims 1, 3, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Schroder et al. (PTO-892; Reference V).

Schroder et al. teaches a method comprising obtaining a skin sample comprising fibroblasts from a human patient, and detecting the activation of fibroblasts by measuring the level of the chemotactic cytokine RANTES expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for RANTES (In particular, abstract, paragraph spanning left and right columns on page 2 to page 4,whole document).

The recitations of "a method of detecting Graves' Disease," "by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)" and "wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease" of claim1; "wherein an elevated level of the marker compared to the control indicates presence of said IgG-activated fibroblasts" of claim 3; and"detecting the presence of antibody-activated fibroblasts" and "detects the presence of antibody-activated fibroblasts" of claim 10 are inherent in the reference method.

The same methods steps are being performed using the same sample (skin fibroblasts) from the same patients (human patients), so the same result must necessarily occur.

The reference teachings anticipate the claimed invention.

11. Claims 1, 3, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Fukuoka et al. (PTO-892; Reference W).

Fukuoka et al. teaches a method comprising obtaining dermal fibroblasts from a human patient, and detecting the activation of fibroblasts by measuring the level of the chemotactic cytokine RANTES expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for RANTES (In particular, abstract, 'Methods' section, whole document).

The recitations of "a method of detecting Graves' Disease," "by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)" and "wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease" of claim1; "wherein an elevated level of the marker compared to the control indicates presence of said IgG-activated fibroblasts" of claim 3; and "detecting the presence of antibody-activated fibroblasts" and "detects the presence of antibody-activated fibroblasts" of claim 10 are inherent in the reference method. The same methods steps are being performed using the same sample (dermal skin fibroblasts) from the same patients (human patients), so the same result must necessarily occur.

The reference teachings anticipate the claimed invention.

12. Claims 1, 3, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Noso et al. (PTO-892; Reference X).

Noso et al. teaches a method comprising obtaining foreskin dermal fibroblasts from a human patient, and detecting the activation of fibroblasts by measuring the level of the chemotactic cytokine RANTES expressed by said fibroblasts relative to a normal control patients by ELISA using an antibody specific for RANTES (In particular, abstract, 'Culture of dermal fibroblasts' section on page 1947, 'Determination of RANTES and GM-CSF immunoreactivity in HPLC fractions' section on page 1948, whole document).

The recitations of "a method of detecting Graves' Disease," "by binding of disease specific IgG to the IGF-1 receptor (IGF-1R)" and "wherein an increased presence of IgG-activated fibroblasts compared to the control indicates Graves' disease" of claim1; "wherein an elevated level of the marker compared to the control indicates presence of said IgG-activated fibroblasts" of claim 3; and "detecting the presence of antibody-activated fibroblasts" and "detects the presence of antibody-activated fibroblasts" of claim 10 are inherent in the reference method. The same methods steps are being performed using the same sample (dermal skin fibroblasts) from the same patients (human patients), so the same result must necessarily occur.

The reference teachings anticipate the claimed invention.

11. Claims 1 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schroder et al. (PTO-892; Reference V), Fukuoka et al. (PTO-892; Reference W) and Noso et al. (PTO-892; Reference X) each in view of U.S. Patent 5,766,866 (PTO-892; Reference B).

Schroder et al., Fukuoka et al. and Noso et al. have all been discussed *supra*.

U.S. Patent 5,766,866 teaches measuring lymphocyte chemoattractant factor in biological samples by ELISA or Western blot using an antibody specific for lymphocyte chemoattractant factor. (In particular, claims 3-5, column 4, lines 42-49, whole document). The reference also teaches measuring functional lymphocyte chemoattractant factor secretion by cells by measuring T cell chemotaxis towards lymphocyte chemoattractant factor, wherein T-cell migration towards lymphocyte chemoattractant factor indicates the presence of functional lymphocyte chemoattractant factor (In particular, column 14, line 51 to column 15, line 19 and column 19, lines 43-67).

It would have been obvious to additionally perform a T cell chemotaxis assay as taught by U.S. Patent 5,766,866 in addition to measuring RANTES secreted by fibroblasts using an ELISA as taught by Schroder et al., Fukuoka et al. and Noso et al. because a T cell chemotaxis

assay measures functional protein secretion by the cells. U.S. Patent 5,766,866 teaches that both ELISA and T cell chemotaxis assays are used to measuring lymphocyte chemoattractant factor, a chemotactic cytokine in a biological sample and Schroder et al., Fukuoka et al. and Noso et al. each teach measuring RANTES, which was another known chemotactic cytokine.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

April 22, 2010

Nora M. Rooney
Patent Examiner
Technology Center 1600

/Nora M Rooney/
Examiner, Art Unit 1644